Treatment Outcomes of Tuberculosis and Associated Factors in University of Gondar Teaching Hospital, Northwest Ethiopia

By

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Jimma, Ethiopia

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Abstract

Back ground: *Tuberculosis remains a major global health problem. It causes ill-health among millions of people each year and ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus. Although the implementation of directly observed treatment, short course increases treatment success and decrease transmission of resistant tuberculosis but global tuberculosis incidence is still growing at 1% a year due to the rapid increase in Africa. Several risk factors for poor tuberculosis treatment outcomes have been reported but it is not clear which factors are major contributors to poor outcome of tuberculosis patients especially in the resource limiting countries.*

Objective*: To assess the outcomes of tuberculosis treatment and associated factors in the University of Gondar Teaching Hospital, Northwest Ethiopia.*

Methods: *A five year retrospective cross-sectional study design was employed and data were collected through medical record review. Data were analyzed using Statistical Package for Social Sciences of windows version 16, binary and multiple logistic regression methods were used. P value of less than 0.05 was considered as statistically significant in the final model.*

Results*: Out of the 1584 PTB patients (882 males and 702 females) included all age group, 60.1% had good outcome and 39.9% had poor treatment outcome. In the final multivariate logistic model, the odds of poor treatment outcome was higher among patients weight category (30-39.9Kg) (AOR = 1.51, 95% CI: 1.102-2.065), smear negative pulmonary TB (AOR=3.204, 95% CI: 2.277-4.509), extra pulmonary TB (AOR=3.175, 95% CI: 2.201-4.581), retreatment (AOR = 6.733, 95% CI: 3.235-14.013), HIV positive TB patients (AOR = 1.988, 95% CI: 1.393-2.838),unknown HIV status TB patients (AOR=1.506,95% CI: 1.166-1.945) as compared to their respective comparison groups.*

Conclusion: *High proportion of poor outcome was documented. Low body weight, smear negative PTB, EPTB, re-treatment cases, HIV-positive TB patients and unknown HIV-status TB patients were associated factors for poor outcome. Therefore patients at high risk of poor outcome should be identified early.*

Key-words: *tuberculosis, treatment outcome, risk factors, Ethiopia*

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List of Acronyms and Abbreviation

AIDS: Acquired Immune Deficiency Syndrome

ART: Anti-Retroviral Treatment

CPT: Cotrimoxazole Preventive Treatment

DOTS: Directly Observed Treatment, Short Course

EPTB: Extra pulmonary Tuberculosis

FMOH: Federal Ministry of Health

HAART: Highly Active Anti Retroviral Treatment

HBC: High-Burden Country

HIV: Human Immunodeficiency Virus

JU: Jimma University

NTLCP: National Tuberculosis & Leprosy Control Programme

NTPs: National Tuberculosis Programme

PTB: Pulmonary Tuberculosis

SPSS: Statistical Package for Social Sciences

TB: Tuberculosis

UoG: University of Gondar

UoGTH: University of Gondar Teaching Hospital

WHO: World Health Organization

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1. INTRODUCTION

1.1. Back ground

According to the 2012 global tuberculosis report, tuberculosis remains a major global health problem. It causes ill-health among millions of people each year and ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV). The latest estimates included in this report are almost 9 million new cases in 2011 and 1.4 million tuberculosis (TB) deaths (990,000 among HIV negative people and 430,000 HIV-associated TB deaths) (1). Geographically, the burden of TB is highest in Asia and Africa. The African Region has 24% of the world's cases and the highest rates of cases and deaths per capita (1).

The World Health Organization (WHO) declared TB a global public health emergency in 1993. Starting in the mid-1990s, efforts to improve TB care and control intensified at national and international levels. WHO developed the Directly Observed Treatment, Short Course (DOTS) strategy within a decade, almost all countries had adopted the strategy and there was considerable progress towards global targets established for 2005 (1).

The growing HIV epidemic represents a great challenge for the National tuberculosis programs, which are seeing an increase in HIV infection among TB cases and the appearance of new TB cases among persons infected with HIV. This is compromising health system performance and National tuberculosis program efficiency due to increased TB incidence, case-fatality, treatment abandonment, and challenges for the comprehensive treatment of both diseases (2).Challenges in the management of TB and HIV co-infected individual is Pill burden, increase adverse effect, drug to drug interaction and immune reconstitution inflammatory syndrome. HIV/AIDS has a number of impacts on prevention and control of TB (3). Tuberculosis is an obstacle to socio-economic development; 75% of people affected by TB are within the economically productive age group of 15-54 years. The HIV epidemic worsened the TB situation and it is estimated that 50 to 60% of HIV infected people will develop TB disease in their lifetime in contrast with HIV negative persons, whose lifetime risk is only 10% (4).

The treatment outcome of new cases of smear-positive pulmonary TB among WHO's six regions, three met or exceeded the 85% target: the Eastern Mediterranean Region, the South-East Asia Region and the Western Pacific Region. The treatment success rate was 82% in the African Region (where there has been steady improvement since 1999), 77% in the Region of the Americas (where the rate has been relatively stable since 2002) and 67% in the European Region (where major efforts to increase treatment success rates are needed). On the other hand the treatment outcome of all new cases among WHO's six regions, the highest rates were in the Eastern Mediterranean (88%), South- East Asia (89%) and Western Pacific (92%) regions.

The treatment success rate was 73% in the African Region, 74% in the Region of the Americas and 74% in the European Region. Among the 22 HBCs Ethiopia is the one and rates of treatment success of new cases of smear-positive pulmonary TB and all new cases in 2010 were (83%) and (77%), respectively (1). In Ethiopia a standardized TB prevention and control program, incorporating DOTS, was started in 1992 (4).

According to the WHO treatment guide line the essential anti-TB drugs are isoniazide, rifampicin, Pyrazinamide, Ethambutol and Streptomycin. All anti-TB drugs should be quality-assured, and management of anti-TB drugs should be incorporated into the management of other essential medicines by the ministry of health (5).

First line treatment of TB in Ethiopia is Rifampicin (R); Ethambutol (E); Isoniazid (H); Pyrazinamide (Z); Streptomycin (S). The drugs available in fixed dose combination and available as single drugs (4). The treatment of TB has two phases: Intensive (initial) and Continuation phase. This phase consists of three or more drugs for the first 8 weeks for new cases, and 12 weeks for re-treatment cases. Continuation phase requires at least two drugs, to be taken for 4 – 6 months. During the continuation phase, the drugs must be collected every month and self-administered by the patient, except for retreatment cases and for regimens containing Rifampicin (4).

A better understanding of the predictors and prognostic factors would allow closer follow-up and more targeted interventions to improve TB treatment outcome, thus reducing TB associated morbidity and mortality. The aim of the present study was to assess the outcome of TB treatment and to identify factors associated with TB treatment outcome in UoGTH Northwest Ethiopia.

1.2. Statement of the Problem

There were an estimated 8.8 million incident cases of TB globally in 2010, 1.1 million deaths among HIV-negative cases of TB and an additional 0.35 million deaths among people who were HIV-positive. In 2009, there were an estimated 9.7 million children who were orphans as a result of parental deaths caused by TB (6). TB is the leading killer among HIV-infected people with weakened immune system, a quarter of a million TB deaths are HIV associated, with most of them in Africa and 98% of TB deaths in the developing world affecting mostly young adults in their most productive years (7).

Although the implementation of DOTS increases treatment success and decrease transmission of resistant tuberculosis but TB kills 5000 people, every day (7-9).Global TB incidence is still growing at 1% a year due to the rapid increase in Africa and especially affects the most vulnerable such as the poorest and malnourished (7).

The World Health Organization declared TB a global public health emergency in 1993 and developed the DOTS strategy, a five-component package. Within a decade, almost all countries had adopted the strategy and there was considerable progress towards global targets established for 2005: the detection of 70% of the estimated number of smear-positive pulmonary cases (the most infectious cases) and the successful treatment of 85% of these cases. In 2005, the numbers of cases reported by NTPs grew to over 5 million and treatment success rates reached 85 % (1).

There is also a finding that shows the magnitude of TB burden in different parts of the world. A retrospective study conducted in Turkey in 2008 on the treatment outcomes of pulmonary TB and factors affecting treatment outcomes. The burden of TB in these finding accounts defaulted treatment 5.1%, died 2.4% failure 0.3% and transferred out 0.5% of all patients and among smear positive pulmonary TB defaulted treatment 5.4%, died 2.9%, failure 0.4% and transferred out 0.7% (10). Similarly defaulted treatment, died, failure and transferred out are the real challenges for TB treatment (11-15).

According to the 2008 report of WHO, Ethiopia ranks seventh among the world's 22 countries with a high tuberculosis burden (16). The Ethiopian Federal Ministry of Health (FMOH) hospital statistics data has shown that tuberculosis is the leading cause of morbidity, the third cause of hospital admission, and the second cause of death in Ethiopia, after malaria (4).

Based on the 2006 WHO estimate in Ethiopia, the incidence of TB of all forms and smear positive TB stand at 378 and 168 per 100,000 populations, respectively. The prevalence and mortality of tuberculosis of all forms is estimated to be 641 and 83 per 100,000 populations respectively (16). A five year retrospective study done in university of Gondar teaching hospital on the treatment outcomes of TB and the treatment success rate of tuberculosis patients was unsatisfactorily low (29.5%). A high proportion of patients died (10.1%) or defaulted (18.3%), which is a serious public health concern that needs to be addressed urgently (17).

Several reasons and risk factors for poor TB treatment outcomes have been reported. Old age, male sex, low income, no or limited access to transport, distance from home to the treatment centre, incomplete treatment compliance, limited interest in information about the disease and its treatment, limited social support, multidrug resistance and co morbidity have all been found to be related to unsuccessful treatment outcomes (12, 18-23).

It is not clear which factors are major contributors to poor outcome of TB patients in the UoGTH. Therefore, it would be better to look for ways of predicting TB treatment outcome and identifying factors that can help to predict poor treatment outcome which will help to identify those patients that are at a higher risk of poor treatment outcome while being treated with anti-TB drugs. With this information, clinicians could give such patients special attention during their follow-up in order to prevent occurrence of negative consequences following poor treatment outcome. This study will assess the TB treatment outcome and the possible associated factors with treatment outcome among TB patients in UoGTH.

2. LITERATURE REVIEW

2.1. Literature Review

Monitoring the outcome of tuberculosis treatment and understanding the specific reasons for poor treatment outcome are important in evaluating the effectiveness of tuberculosis control program. There are factors associated with poor TB treatment outcome. The following literatures were reviewed to assess those factors. I try to divide literature review: 1) socio-demographic factors 2) Co-morbidity related factors 3) Tuberculosis type, Category of patient and treatment regimen factors.

1. Socio-demographic factors

Most literatures discussed that the risk of poor treatment outcome to TB is increasing with age and being male also a risk factor (12, 24-25). A retrospective survey conducted in northeastern Thailand showed that the risk of treatment failure/death were age greater than 60 years, and history of previous TB treatment (18). Male sex and care provided by a non-pulmonary physician were independent factors significantly associated with treatment interruption (18).

A five year retrospective study done in the Southern Region of Ethiopia in 2010 on the factors associated with poor tuberculosis treatment outcome. A study found that age >55 years, male sex, treatment, being on retreatment, having a positive smear after 2 months of treatment and a diagnosis of smear-negative PTB were independently associated with a poor outcome (19). Similar findings in Finland with cohort study also identified male sex, high age as risk factors for deaths (11).

A retrospective cohort study conducted in Addis Ababa in 2011 on the mortality and associated risk factors in a cohort of tuberculosis patients treated under DOTS program. The findings of these study were the body weight at initiation of anti-TB treatment (<35 kg), patient category, year of enrollment and treatment center were independent predictors for time to death (26). In other finding higher weight at treatment initiation was protective (27).

A case control study done in remote poor areas of China stated that being illiterate, being farmer, not having a job, fever and loss of appetite as initial symptoms, diagnosis of TB outside the CDC, not having a treatment observer, missing more of the TB drugs, interrupted treatment, having side effects during treatment, no or irregular sputum examinations were statistically

significant association with a lower cure rate (12). Interruption of treatment was most strongly associated with non-cure and having side effects was the main reason for interrupting treatment (46.5%) (12). An observational study with a retrospective cohort in India showed that factors independently associated with default were alcoholism, illiteracy, and important commitments (28).

2. Co-morbidity related factors

A study conducted in Brazil with a retrospective cohort design in 2012, studied the effect of HIV on outcomes of TB treatment. The result found that treatment outcomes were best for those HIV negative cases and worst for those known HIV positive patients (cure rate of 85.7% and 55.7% respectively) (29). The risk of having an unfavorable outcome (all outcomes except cure) was 3.09 times higher for those HIV positive compared with those HIV negative and the risk of death and default also increased with HIV positivity (29).

A retrospective cohort study conducted on the factors associated with unsuccessful TB treatment outcomes on HIV infected TB patients in Giang province, Vietnam, 2001-2004. Patients who used co-trimoxazole prophylaxis therapy were less likely to have unsuccessful treatment outcome and patients had adverse event during TB treatment were more likely to have unsuccessful treatment outcome (30). Other finding in south India on the treatment outcome and mortality at one and half year follow-up of HIV infected TB patients under TB control program showed that factors significantly associated with unfavorable outcome were disease classification as pulmonary, type of patient as retreatment, and non initiation of ART. Factors associated with death were no initiation of ART and CPT (31).

A retrospective survey conducted in Northeastern Thailand in 2005 studied factors associated treatment outcomes in pulmonary TB. Factors related to treatment outcome in smear positive pulmonary tuberculosis were evaluated in 226 adult patients. The study found that the risk of treatment failure/death were presence of HIV-co-infection in addition to old age, history of previous TB treatment, and male sex (18).

3. TB type and Category of patient

Retrospective study conducted in Southern Region of Ethiopia on the Factors associated with poor tuberculosis treatment outcome. The result showed that being on retreatment, having a positive smear at the second month follow-up, and having smear-negative pulmonary TB were independent risk factors for poor outcome (19). Similarly study in Tigray region also found that unsuccessful treatment outcome was higher among retreatment cases (32).

A cohort study in Finland in 2010 was using patients data registered from January 1st, 1995, to December 31st, 1996 and studied treatment outcome of extra-pulmonary tuberculosis. The study were included a total of 1059 patients and result found that male sex, high age, immunosuppression, any other than a pulmonary specialty and other than standard combination of treatment were significant independent risk factors for death (33). For other unfavorable treatment outcomes, significant risk factor was treatment with INH + RIF + EMB/SM (33).

A retrospective cohort study done in Addis Ababa on the mortality and associated risk factors in tuberculosis patients treated under DOTS program. The studied found that proportion of death from pulmonary positives, pulmonary negatives and extra pulmonary TB patients were 2.7%, 3.6%, and 4.3%, respectively (26). The body weight at initiation of anti-TB treatment (<35 kg), patient category, year of enrollment and treatment center were independent predictors for time to death and also retreated TB patients were 1.74 times more likely to die compared to new TB patients (26).

A retrospective cohort study was conducted in Morocco in 2011 to study risk factors for tuberculosis treatment failure, default, or relapse and outcomes of retreatment. The result found that male gender, positive sputum smear after 3 months of treatment, and hospitalization were independent risk factors for failure, default, or early relapse after initial treatment and male sex, substance use, missed doses, and hospitalization appeared to be risk factors for default (27).

2.2. Conceptual frame work

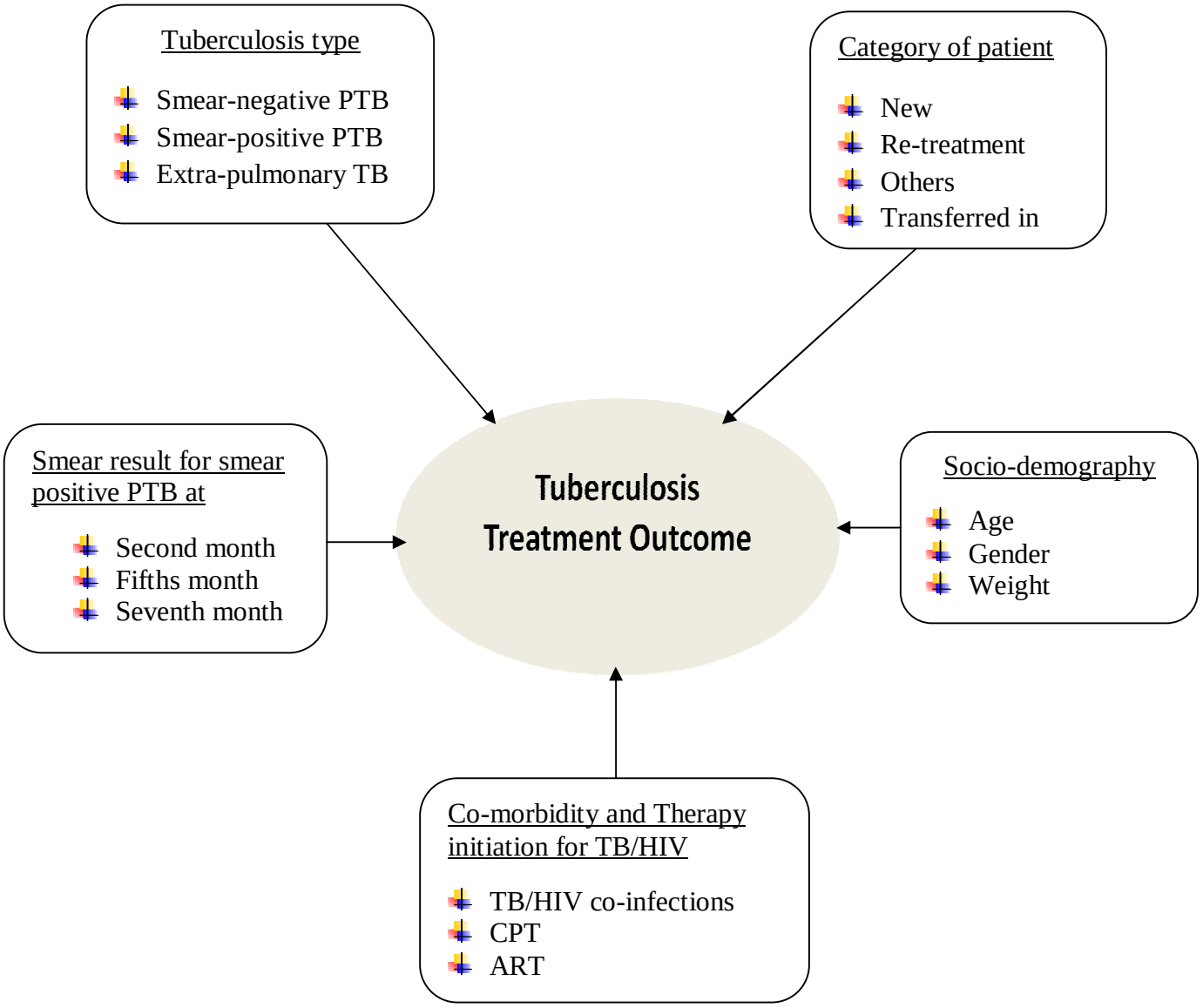


Figure 1: Conceptual frame work for factors associated with tuberculosis treatment outcome.

(Source: developed by principal investigator based on literature review)

According to the different findings socio-demography, co-morbidity and type of TB affect treatment outcome. Being male, old age and low body weight contribute to poor outcome of TB. TB/HIV co-infection associated with poor outcome than patients who have TB alone. On the other hand smear positive PTB had better outcome than smear negative PTB and EPTB.

2.3. Significance of the study

The findings of the study may in general help the health management at higher level and health institutions level to understand the extent of the problem. The study will enhance the capacity to look for possible alternative solutions to health service with regard to associated factors with poor TB treatment outcome in collaboration with the health centers, hospitals and relevant stake holders. It will have also contribution to increase the knowledge about TB and associated factors with poor TB treatment outcome in the areas by concerned bodies including the health center and hospital staffs so as to develop strategies to alleviate this problem.

In addition, the study may be useful to other researchers as springboard while conducting further studies on similar problems. Identification of associated factors with poor TB treatment outcome is also essential in order to guide program planning, and organizing health service. It is expected that identifying those risk factors will enable to improve treatment outcome and increase success rate set by WHO in Ethiopia particularly in University of Gondar Teaching Hospital.

3. OBJECTIVE

3.1. General Objective

To assess the outcomes of patients registered for anti-tuberculosis treatment and to assess associated factors in the University of Gondar Teaching Hospital, Northwest Ethiopia.

3.2. Specific Objectives

- To assess the outcomes of patients registered for anti-tuberculosis treatment.
- To identify associated factors with poor treatment outcomes of tuberculosis.

4. METHODS AND PARTICIPANTS

4.1. Study Area and period

Gondar is the ancient town located in the Semien Gondar Zone of the Amhara Region, Northwest Ethiopia and 727km. far from Addis Ababa. The study was conducted in University of Gondar teaching hospital found in Gondar town. The hospital provides health services for the population of Gondar town and remote areas of northwest Ethiopia. The total population served by the hospital is more than 5 million. In the hospital DOTS clinic is operating under the NTLCP of Ethiopia. The data were collected from March 03 to April 8/2013.

4.2. Study design

Retrospective cross-sectional study was employed.

4.3. Source population

The source population of the study was all patients registered for treatment of TB at University of Gondar Teaching Hospital from 1st September 2008 and 31st August 2012.

4.4. Study participants

The study population was all tuberculosis patients who had treatment outcome at University of Gondar Teaching Hospital between 1st September 2008 and 31st August 2012.

Inclusion criteria

- Full patient data
- New case
- Re-treatment case
- Others
- Transfer in
- PTB/EPTB

Exclusion criteria

- TB patients who had two outcome
- Transferred out patients

4.5. Sample size and sampling technique/procedure

All data were retrieved from records of patient registration who took anti TB treatment during the period of 1st September 2008 and 31st August 2012.

4.6. Variables in the study

Dependent variables

Tuberculosis treatment outcome

Independent variables

- Socio-demography
  - Age
  - Gender
  - weight
- Co-morbidity
  - TB/HIV co infections
- Tuberculosis type
  - Smear-negative pulmonary TB
  - Smear-positive pulmonary TB
  - Extra-pulmonary TB
- Category of patient
  - New case
  - Re-treatment case
  - Others
  - Transferred in

4.7. Data collection and Data quality

Data were collected through medical record reviews of patients using a prepared standard checklist in TB clinic. The content of the checklist include socio-demography, HIV status, types of TB and treatment outcome. In order to assure the quality of data the following measures were be undertaken:-

- Data was collected by 4 nurses after giving one day training for data collectors on the data collection format and techniques of data collection. Supervisor was strictly supervising data collectors daily and the principal investigator was reviewing all filled format.

4.8. Data processing and analysis

Data were checked for its completeness every day. To be edited, cleaned and analyzed, the collected data were entered into a computer using SPSS version 16. A descriptive analysis was conducted to check for outliers, consistencies and to identify missed values for independent variables. Bivariate analysis was employed to see the crude association between each exposure versus outcome variables. To control the effect of confounding factors or to get independently associated variables, each variables that are statistically significant at p –value <0.2 in bivariate analysis was entered in to backward stepwise multiple logistic regression model as the independent variable and TB treatment outcome status being a dependent variable. $P < 0.05$ was considered as statistically significant for all the independent variables in the final model.

4.9. Ethical consideration

Letter of ethical clearance was obtained from Research Ethics Committee of Jimma University. The patient data were accessed upon the approval of clinical director of UoGTH. Confidentiality was ensured during the data collection, thus name and address of the patient was not recorded in the data collection check list.

4.10. Dissemination plan

The result of the study will be disseminated to responsible bodies such as Jimma university department of Pharmacy, Federal Ministry of Health, Ethiopia Food, medicines and health care Administration and Control Authority, Regional health bureau, zonal and district health offices and district administration of the study area. The study finding will also be submitted to professional journal for publication so as to serve as base line for further studies.

4.11. Definitions of terms

According to the standard definitions of the National Tuberculosis and Leprosy Control Program guideline (NLCP) adopted from WHO, the following clinical case and treatment outcome definitions were used:

Smear-positive pulmonary TB

A patient with at least two sputum specimens which were positive for acid-fast bacilli (AFB) by microscopy, or a patient with only one sputum specimen which was positive for AFB by microscopy, and chest radiographic abnormalities consistent with active pulmonary TB.

Smear-negative pulmonary TB

A patient with symptoms suggestive of TB, with at least two sputum specimens which were negative for AFB by microscopy, and with chest radiographic abnormalities consistent with active pulmonary TB (including interstitial or miliary abnormal images), or a patient with two sets of at least two sputum specimens taken at least two weeks apart, and which were negative for AFB by microscopy, and radiographic abnormalities consistent with pulmonary TB and lack of clinical response to one week of broad spectrum antibiotic therapy.

Extra-pulmonary TB (EPTB)

This included tuberculosis of organs other than the lungs, such as lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges, etc. Diagnosis of EPTB was based on fine needle aspiration cytology or biochemical analyses of cerebrospinal/pleural/ascitic fluid or histopathological examination or strong clinical evidence consistent with active extrapulmonary tuberculosis, followed by a decision of a clinician to treat with a full course of anti-tuberculosis chemotherapy. In all the cases of EPTB, sputum examinations and chest radiographs were used to investigate the involvement of lung parenchyma.

A case of TB is a patient in whom tuberculosis has been confirmed bacteriologically or diagnosed by a clinician. The following are case definitions:

- **New case (N):** A patient who never had treatment for TB, or has been on previous anti-TB treatment for less than four weeks.

- **Relapse (R):** A patient declared cured or treatment completed of any form of TB in the past, but who reports back to the health service and is now found to be AFB smear-positive or culture positive.
- **Treatment Failure (F):** A patient who, while on treatment, is smear-positive at the end of the fifth month or later, after commencing. Treatment failure also includes a patient who was initially sputum smear-negative but who becomes smear-positive during treatment.
- **Return after default (D):** A patient previously recorded as defaulted from treatment and returns to the health facility with smear-positive sputum.
- **Transfer out (T):** A patient who started treatment in one treatment unit and is transferred to another treatment unit to continue treatment.
- **Chronic (C):** A TB patient who remains smear-positive after completing a retreatment regimen.
- **Other (O):** A patient who does not fit in any of the above mentioned categories (e.g., a PTB smear negative who returns after treatment interruption).

Treatment Outcome

The treatment outcome was divided into seven categories according to NTLCP guideline. These categories were:

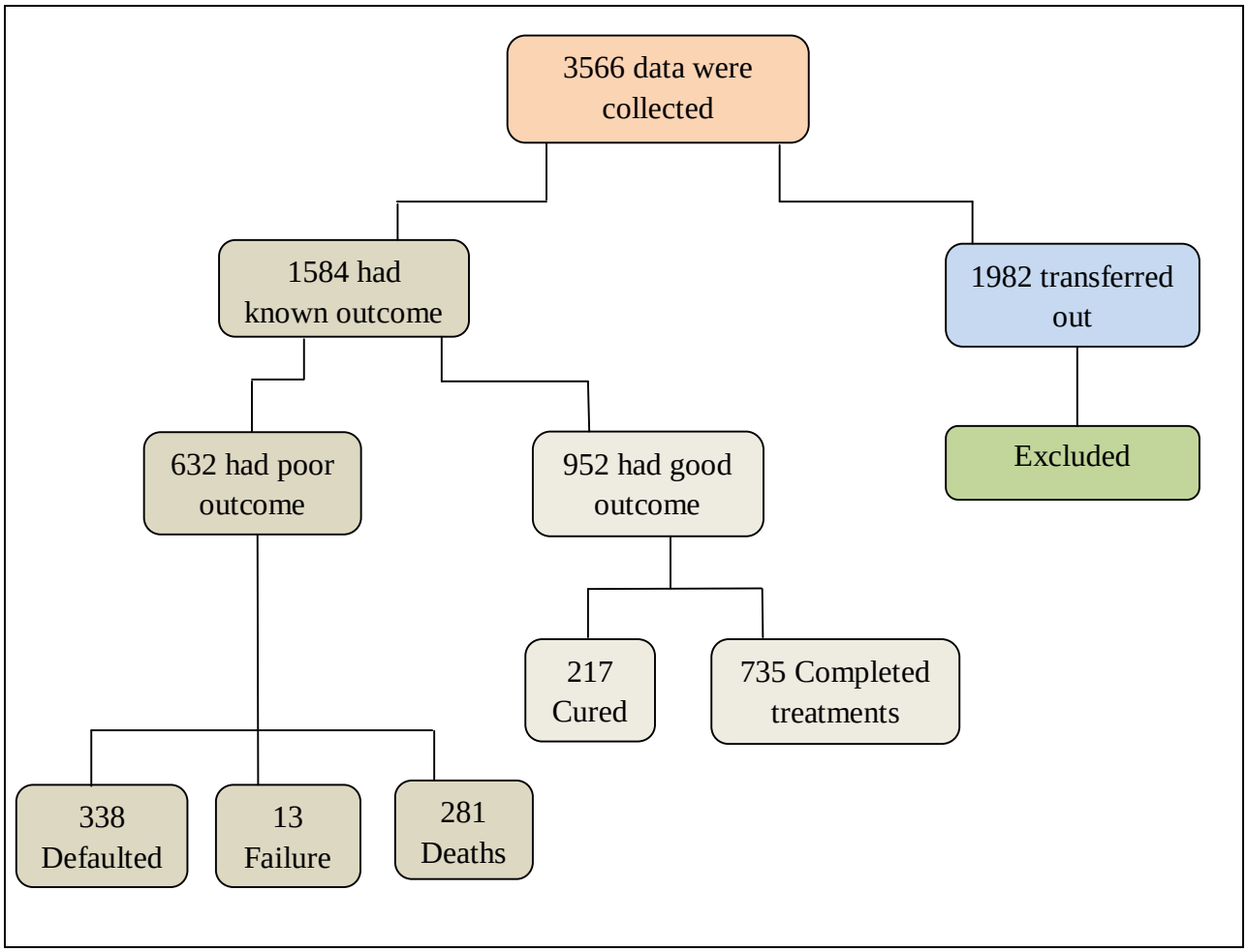
- **Cured:** Finished treatment with negative bacteriology result at the end of treatment.
- **Completed treatment:** Finished treatment, but without bacteriology result at the end of treatment.
- **Failure:** remaining smear positive at five months despite correct intake of medication.
- **Defaulted treatment:** Patients who interrupted their treatment for two consecutive months or more after registration.
- **Died:** Patients who died from any cause during the course of treatment.
- **Transferred out**: Patients whose treatment results are unknown due to transfer to another health facility and
- **Successfully treated**: A patient who was cured or completed treatment.

In line with WHO criteria, treatment outcomes were categorized into:

- Good outcome- if TB patients were cured (i.e., negative smear microscopy at the end of treatment and on at least one previous follow-up test) or completed treatment with resolution of symptoms.
- Poor outcome – if treatment of TB patients resulted in treatment failure (i.e., remaining smear-positive after 5 months of treatment), default (i.e., patients who interrupted their treatment for two consecutive months or more after registration), or death.

However, patients who transferred out to other districts were excluded from the treatment outcome evaluation as information on their treatment outcome was unavailable.

5. RESULT



5.1. Socio-demographic and clinical characteristics

Out of 1584 patients who had known outcome between January 2008 and December 2012 at University of Gondar Teaching Hospital, 882 (55.7%) were males and their mean age was 28.3 (SD ±1.47) years (Table 1). Among patients for whom disease category were documented 303 (19.1%) smear-positive and 844 (53.3%) smear-negative TB (PTB). Category of patients were also documented for all type of TB, of these 1307 (82.5%) were classified as new cases. With regard to HIV status, 212 (13.4%) were positive and of those HIV-positive, 54 (25.5%) and 45 (21.2%) initiated CPT and ART respectively. Concerning with smear result, 32(10.6%) was positive at the second month. (Table 2)

Table 1 Socio-demographic characteristics of all TB patients in UoGTH, 2008-2012

Characteristics	Frequency	Percent
Age(years)		
<15	211	13.3
≥15	1373	86.7
Sex		
Male	882	55.7
Female	702	44.3
Weight(Kg)		
0-4.9	14	0.9
5-7.9	31	2.0
8-14.9	60	3.8
15-19.9	35	2.2
20-29.9	65	4.1
30-39.9	216	13.6
40-54.9	831	52.2
55-70.9	238	15.0
≥71	16	1.0
Unknown	78	4.9

Table 2 Clinical characteristics of all TB patients in UoGTH, 2008-2012

Characteristics	Frequency	Percent
Tuberculosis type		
smear positive	303	19.1
smear negative	844	53.3
extra pulmonary	437	27.6
Category of patients		
New	1307	82.5
Retreatment	41	2.6
Other	89	5.6
Transfer in	147	9.3
HIV status		
Positive	212	13.4
Negative	420	26.5
unknown	952	60.1
CPT initiation for HIV-positive TB patients		
Yes	54	25.5
No	158	74.5
ART initiation for HIV-positive TB patients		
Yes	45	21.2
No	167	78.8
Smear result at 2nd month for PTB +ve patients		
Positive	32	10.6
negative	207	68.3
Not tested	64	21.1
Smear result at 5th month for PTB +ve patients		
Positive	5	1.7
negative	221	72.9
Not tested	77	25.4
Smear result at 7th month for PTB +ve patients		
Positive	3	1.0
negative	218	71.9
Not tested	82	27.1

5.2. Treatment outcome of all TB patients in UoGTH, 2008-2012

Among all TB patients enrolled in this study 735 (46.4%) completed treatment, 338 (21.3%) defaulted, 281 (17.7%) died, 217 (13.7%) cured, 13 (0.8%) treatment failure (Table 3). From the 1584 patients evaluated for treatment outcome, 952 (60.1%) had good outcome and 632 (39.9%) poor outcomes (Table 4). Of the patients with poor treatment outcome, 281 (17.7%) had died, 13 (0.8 %) had treatment failure and 338 (21.3%) had defaulted (Table 3)

Table 3 Outcomes of all TB patients by age, sex and year of registration in UoGTH

Characteristics	Total (n=1584)	Cured	Treatment completed	Death	Failure	Default
Age(years)						
<15	211	2	125	14	0	70
≥15	1373	215	610	267	13	268
Sex						
Male	882	119	415	158	6	184
Female	702	98	320	123	7	154
Year of registration						
2008	419	69	173	97	7	73
2009	348	49	161	61	1	76
2010	285	33	138	47	2	65
2011	296	35	124	44	3	90
2012	236	31	139	32	0	34

5.3. Treatment outcome of TB and crude association with outcome

Bivariate logistic regression analysis was carried out for all patients who had outcome but transferred out patients are exclude in the analysis. In socio-demographic characteristics weight has association but age and sex does not have association with treatment outcome. Clinical characteristics including tuberculosis type, category of patients, HIV status, CPT initiation, ART initiation and smear result at second, fifth and seventh months have association with treatment outcome (Table 4).

Table 4 Bivariable logistic regression analysis and association with treatment outcome in all type of TB patients in UoGTH, 2008-2012

Characteristics	Good outcome n (%)	Poor outcome n (%)	COR (95%CI)	P-value
Age(years)				
<15	127(60.2)	84(39.8)	0.996(0.741-1.339)	0.977
≥15	825(60.1)	548(39.9)	1	
Sex				
Male	534(60.5)	348(39.5)	1	
Female	418(59.5)	284(40.5)	1.043(0.852-1.276)	0.686
Weight(kg)				
0-4.9	4(28.6)	10(71.4)	3.61(1.123-11.606)	0.031
5-7.9	12(38.7)	19(61.3)	2.287(1.096-4.772)	0.028
8-14.9	36(60)	24(40)	0.963(0.564-1.643)	0.889
15-19.9	23(65.7)	12(34.3)	0.753(0.370-1.535)	0.436
20-29.9	42(64.6)	23(35.4)	0.791(0.467-1.339)	0.383
30-39.9	104(48.1)	112(51.9)	1.555(1.151-2.101)	0.004
40-54.9	491(59.1)	340(40.9)	1	
55-70.9	168(70.6)	70(29.4)	0.602(0.441-0.821)	0.001
≥71	14(87.5)	2(12.5)	0.206(0.047-0.914)	0.038
unknown	58(74.4)	20(25.6)	0.498(0.294-0.843)	0.009
Tuberculosis type				
smear positive	224(73.9)	79(26.1)	1	
smear negative	469(55.6)	375(44.4)	2.267(1.696-3.030)	0.000
extra pulmonary	259(59.3)	178(40.7)	1.949(1.416-2.683)	0.000
Category of patients				
new	772(59.1)	535(40.9)	1	
retreatment	13(31.7)	28(68.3)	3.108(1.595-6.055)	0.001
others	54(60)	36(40)	0.980(0.633-1.518)	0.928
Transfer in	113(77.4)	33(22.6)	0.418(0.279-0.625)	0.000

HIV status				
positive	105(49.5)	107(50.5)	2.223(1.584-3.121)	0.000
negative	288(68.6)	132(31.4)	1	
Not tested	559(58.7)	393(41.3)	1.534(1.203-1.956)	0.001
CPT initiation for HIV-positive				
yes	33(61.1)	21(38.9)	0.533(0.284-1.001)	0.050
no	72(45.6)	86(54.4)	1	
ART initiation for HIV-positive				
yes	28(62.2)	17(37.8)	0.519(0.264-1.020)	0.057
no	77(46.1)	90(53.9)	1	
Smear result at 2nd month for smear positive PTB				
Positive	20(62.5)	12(37.5)	0.086(0.031-0.240)	0.000
negative	196(94.7)	11(5.3)	0.008(0.003-0.021)	0.000
Not tested	8(12.5)	56(87.5)	1	
Smear result at 5th month for smear positive PTB				
Positive	1(16.7)	5(83.3)	0.672(0.070-6.417)	0.730
negative	214(96.8)	7(3.2)	0.004(0.002-0.012)	0.000
Not tested	9(11.8)	67(88.2)	1	
Smear result at 7th month for smear positive PTB				
Positive	0	3(100)	NA	
negative	217(99.5)	1(0.5)	0.000(0.000-0.004)	0.000
Not tested	8(9.6)	74(90.4)	1	

NA=not applicable, COR= Crude Odds Ratio, 1: indicates reference

5.4. Treatment outcome of TB and factors independently associated with outcome

Logistic regression analysis was carried out for socio-demographic and clinical characteristics including age, sex, weight, tuberculosis type, category of patients, HIV status, CPT initiation, ART initiation and smear result at second, fifth and seventh months. In the final multivariable logistic model, poor treatment outcome varied by weight, tuberculosis type, and category of patients, HIV status (Table 5).

The probability of developing poor treatment outcome was 1.508 (95% CI: 1.102-2.065) times higher among weight category 30-39.9kg compared to 40-54.9kg.Weight categories 50-70.9kg of TB patients were less likely to experience (AOR = 0.573, 95% CI: 0.415-0.790) poor outcome than weight categories of 40-54.9kg. Good outcome were documented in weight category ≥71kg than weight category 40-54.9kg (AOR = 0.199, 95% CI: 0.044-0.897).Patients who were being treated for smear negative PTB had 3.204, (95% CI: 2.277-4.509) times poor outcome than patients being treated for smear positive PTB. A type of TB documented as EPTB had also 3.175 (95% CI: 2.201-4.581) times higher probability of poor treatment outcome compared to smear positive PTB. The likely hood of poor treatment outcome was more frequent (AOR = 6.733, 95% CI: 3.235-14.013) among retreatment cases than among those newly treated. Category of patients who had transferred in were less likely to experience (AOR = 0.380, 95% CI: 0.214-0.673) poor outcome when compared to those newly treated. Patients who were being treated for HIV-positive TB patients had poor treatment outcome than patients being treated for HIV-negative TB patients (AOR = 1.988, 95% CI: 1.393-2.838). The probability of developing poor treatment outcome was 1.506 (95% CI: 1.166-1.945) times higher among TB patients not tested there HIV-status than HIV-negative TB patients (Table 5).

Table 5 Multivariable logistic regression analysis and factors associated with poor treatment outcome in all type of TB patients in UoGTH, 2008-2012

Characteristics	Good outcome n (%)	Poor outcome n (%)	AOR (95% CI)	P-value
Weight(kg)				
0-4.9	4(28.6)	10(71.4)	2.826(0.868-9.196)	0.084
5-7.9	12(38.7)	19(61.3)	1.909(0.901-4.047)	0.092
8-14.9	36(60)	24(40)	0.830(0.480-1.437)	0.507
15-19.9	23(65.7)	12(34.3)	0.605(0.294-1.245)	0.172
20-29.9	42(64.6)	23(35.4)	0.695(0.403-1.198)	0.191
30-39.9	104(48.1)	112(51.9)	**1.508(1.102-2.065)**	**0.010**
40-54.9	491(59.1)	340(40.9)	1	
55-70.9	168(70.6)	70(29.4)	**0.573(0.415-0.790)**	**0.001**
≥71	14(87.5)	2(12.5)	**0.199(0.044-0.897)**	**0.036**
Unknown	58(74.4)	20(25.6)	1.204(0.573-2.532)	0.624
Tuberculosis type				
Smear positive	224(73.9)	79(26.1)	1	
Smear negative	469(55.6)	375(44.4)	**3.204(2.277-4.509)**	**0.000**
Extra pulmonary	259(59.3)	178(40.7)	**3.175(2.201-4.581)**	**0.000**
Category of patients				
New	772(59.1)	535(40.9)	1	
Re-treatment	13(31.7)	28(68.3)	**6.733(3.235-14.013)**	**0.000**
Others	54(60)	36(40)	0.841(0.536-1.319)	0.451
Transfer in	113(77.4)	33(22.6)	**0.380(0.214-0.673)**	**0.001**
HIV status				
Positive	105(49.5)	107(50.5)	**1.988(1.393-2.838)**	**0.000**
Negative	288(68.6)	132(31.4)	1	
Not tested	559(58.7)	393(41.3)	**1.506(1.166-1.945)**	**0.002**

AOR=Adjusted Odds Ratio, 1: indicates reference

6. DISCUSSION

Assessment of anti-tuberculosis treatment outcome and analysis of factors responsible for poor treatment outcome is one of the major indicators for the evaluation of the performance of a national TB program. In this study, the good outcomes of all TB type were 60.1%, which is lower than the NTLCP and WHO target of 85%, in addition lower than the studies conducted in some parts of Ethiopia including 74.8% in Southern region (19) and 89.0% in Tigray region of Ethiopia (32), but has higher success rate than studies done previously in University Gondar Teaching Hospital (29.5%) (17) and 26% in Felege Hiwot Referral Hospital (34).

In this finding successful outcome increases from the previous 29.5% to 60.1% and this could be due to the exclusion of transferred out patient, because large number of transferred out could compromise the treatment success rate, as this group is often included in the denominator. Here the feedback system is poor and there are no mechanisms to confirm whether these patients registered to continue treatment in other centers. The other possible reason for the increment of successful treatment outcome in UoGTH compared to the previous study conducted in this university hospital could be the encouragement of DOTS performance.

The 39.9% poor outcome found in this study is comparatively lower than the 70.6% report from previous study conducted in UoGTH (17) and 76% in Felege Hiwot Referral Hospital (34). The 21.3% default, 17.7% death rate and 0.8 % treatment failure recorded in this study is also lower when compared with the corresponding outcomes from Southern region of Ethiopia, where 60.9% patients had defaulted, 36.9% had died and 2.2% failed treatment(19); this could be study participant variation in the two study. Compared to this data, studies done in other parts of the world recorded lower proportion of poor outcome (10-11, 25). This difference could be due to variation in DOTS performance in the various study areas. There was little knowledge about TB, inappropriate health seeking behavior and stigma towards TB in the Gilgel Gibe field research area (20) this could be other possible reason for the difference.

In multivariable logistic regression model, this study showed that poor treatment outcome was significantly higher among patients weight category 30-39.9kg, smear negative PTB and EPTB, among those re-treatment cases, sero-positive TB patients and unknown sero-status TB patients.

But poor treatment outcome was significantly lower among patients weight category 55-70.9kg, ≥71kg and transferred in patients.

In this study body weight at initiation of anti-TB treatment (30-39.9kg) was significantly associated with poor treatment outcome but body weight at initiation of anti-TB treatment (55-70.9kg and ≥71kg) was significantly associated with good treatment outcome. One study in Addis Ababa revealed that body weight at initiation of anti-TB treatment (<35 kg) was a significant risk factors of death during anti-tuberculosis treatment period (26). This difference may be related to the classification of body weight at initiation of anti-TB treatment, in this study body weight classification is based on WHO standard treatment guide line but a study conducted in Addis Ababa used other type of body weight classification. Other study also reported that among persons who were underweight at diagnosis, weight gain of 5% or less after two months of treatment was associated with an increased risk of relapse (35).

In this observation tuberculosis type was associated with poor treatment outcome. The characteristics of TB patients associated with poor outcome during anti-TB treatment were being smeared negative pulmonary TB and extra pulmonary TB (19, 34). This could be due to the treatment outcome monitoring of smear-positive pulmonary TB patients are by testing sputum result at 2^{nd}, 5^{th} and 7^{th} in addition to clinical progression of the patients but monitoring the treatment outcome of patients with smear-negative pulmonary TB and extra pulmonary TB is only clinical condition. The number of patients having smear-negative pulmonary TB and extra pulmonary TB were higher than smear-positive pulmonary TB could be another possible justification for poor outcome.

In our study treatment category was associated with poor treatment outcome particularly previously treated patients. One study stated that being retreatment was found to be a significant risk factor for poor treatment outcome (32). Similar findings also reported that re-treatment was significantly correlated with poor treatment outcome (19, 26, 31-32). Thus, the high proportion of poor outcome in retreatment cases in this study could be related to prior sub-optimal therapy and drug resistance. Globally, 3.7% (2.1–5.2%) of new cases and 20% (13–26%) of previously treated cases are estimated to have MDR-TB (1). The proportion of MDR-TB in Ethiopia is (0-2.9%) among new cases and (6-11.9%) among retreatment cases (1).

Unlike re-treatment cases, transferred in patients had good outcome compared to new cases in this finding, good outcome could be associated with large number of patients may not have co-morbidity like HIV. The other possible reason could be patients may have good knowledge about TB and its treatment. There was a lower proportion of treatment success among the transfer-in patients (69%) when compared to non transfer-in patients (83%) as there were more patients with missing treatment outcomes among the transfers-in (27% vs. 8%) (36).

Data from this study revealed that HIV positive TB patients have an increased risk of poor outcome compared to HIV-negative TB patients. This is similar with other published reports, in which TB/HIV co-infection was significantly associated with poor treatment outcome (18, 29, 37). The poor outcome in TB and HIV co-infection patients in this study could be related to pill burden, increase adverse effect, drug to drug interaction and immune reconstitution inflammatory syndrome.

Like TB and HIV co-infected patients unknown HIV status TB patients have also increased risk of poor outcome compared to HIV-negative TB patients. One study conducted in San Francisco stated that significantly large percentage of the HIV-infected patients died than the HIV-uninfected/unknown patients (38). The possible reason of poor outcome in unknown HIV-status TB patients in this study could be, even if there HIV status is not tested these patients might be HIV positive and uninitiated of HAART timely for those HIV-positive TB patients is a contributory factor for poor outcome. Co-morbidity other than HIV may be another possible reason.

The use of HAART during treatment for tuberculosis significantly protected against mortality when compared with HIV-infected patients who did not receive antiretroviral medications or who received regimens other than HAART (38). Similar study stated that HIV infection without the use of ART were a factor reduced the probability of cure (14). HIV-infected patients who received HAART during tuberculosis treatment converted their sputum smears and cultures to negative significantly faster than those not treated with HAART (38).Another study in south India showed that non initiation of ART significantly associated with unfavorable outcome (31).

7. STRENGTH AND LIMITATION OF THE STUDY

Strength of the study

- This study was incorporated large number of patients.
- Identifying of associated factors with poor treatment outcome of TB in the UoGTH.

Limitation of the study

- This was a retrospective study so data were secondary and it was difficult to assess income, educational status and family size.
- Large numbers of patients were transferred out; so it was difficult to assess the outcome.
- Poor documentation.
- The study participants were only patients in UoGTH.

8. CONCLUSIONS

High proportion of poor outcome documented in this study i.e., 281 (17.7%) had died, 13 (0.8 %) had treatment failure and 338 (21.3%) had defaulted and the good outcome is still low as compared to WHO target (85%).

Moreover, the following risk factors were identified as predictors of poor treatment outcome: body weight at initiation of anti-TB treatment (30-39.9kg), smear negative PTB, EPTB, re-treatment cases, HIV-positive TB patients and unknown HIV-status TB patients.

9. RECOMMENDATIONS

Based on the findings of this study, the following recommendations are suggested:

- Low body weight, smear negative PTB, EPTB, TB/HIV co-infection and unknown HIV status TB patients should be identified early.
- Give additional follow-up, home visits, social support and health education.
- HIV/TB co-infected patients initiate ART and CPT timely, counseling during treatment and health education is important to increase good outcome.
- For unknown HIV status TB patients, early screening and health education is also mandatory to decrease poor outcome.
- Economic status, educational status, family size and nutritional status has association with the outcome, so recording such characteristics and studying the effect these variable with outcome is mandatory to increase the good outcome.
- The fate of transferred out patients is not known so it is important to study these patients.

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ANNEXE

Data collection check list

To assess treatment outcome of tuberculosis and risk factors for poor treatment outcomes at University of Gondar Teaching Hospital.

Instruction

A. Select your answer for the questions by marking "√" in the box provided
B. If your answer is out of the choice provided; write your answer in the space provided.

1.	Age of the patient in year	☐
2.	Sex of the patient	Male ☐ Female ☐
3.	Weight of the patient in kilogram	☐
4.	Type of TB	Pulmonary TB ☐ Smear positive PTB ☐ Smear negative PTB ☐ Extra pulmonary TB ☐
5.	Category of patients	New ☐ Re treatment ☐ others ☐ transferred in ☐
7.	Treatment outcome TB	Cured ☐ Completed treatment ☐ Transferred out ☐ Died ☐ Failure ☐ Defaulted ☐
8.	HIV status of the patient	HIV positive ☐ If positive ART initiated? Yes ☐ No ☐ If positive CPT initiated? Yes ☐ No ☐ HIV negative ☐
9.	Smear result	After 2nd month: Smear positive ☐ Smear negative ☐ At 5th months: Smear positive ☐ Smear negative ☐ At 7th months: Smear positive ☐ Smear negative ☐